Ketogenic Diet Basics for the Non-Ketogenic Clinician

An Overview

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Disclosures

- Consultant – Keto Ambassador for Nutricia North America

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Overview

1. History of the Classical Ketogenic Diet (CKD)
2. Overview of the classical ketogenic diet
   - Review the other variants of the classic ketogenic diet
3. Calculate the classic ketogenic diet
4. Identify helpful tips for monitoring patients on the medical ketogenic diet

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What is the ketogenic diet?

- Search results

44,200,000

536,000

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Timeline of the ketogenic diet

Hippocrates

400 BC

1800's

Parisian physicians reported that fasting reduced seizure severity in 20 children and adults with epilepsy

1911

H. Houston Merritt and Tracy Putnam discovered phenytoin (Dilantin®)

1938

With the introduction sodium valporate, the use of the ketogenic diet is restricted to mainly difficult cases.

1970

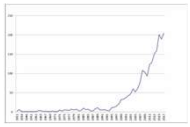
Charlie FOUNDATION

The Charlie Foundation is founded

1994

First Do No Harm is released

1997



Poster abstract presented at the American Epilepsy Society – increased interest in the ketogenic diet

1998

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Ancient Greece

Hippocrates ~400 BC

- Man with body burns and seizures
- "complete abstinence from food and water"

Galen ~200 BC

- Recommended "abstinence from daily use of such food as engenders unhealthy humors"

Mark 9: 14-29

The Bible: King James Version

- "he fell on the ground, and wallowed foaming"
- "he asked his father, How long is it ago since this came unto him? And he said, of a child"
- "Jesus took him by the hand, and lifted him up; and he arose"
- "And he said unto them, this kind can come forth by nothing, but by prayer and fasting"

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Water Diets

- 1800's - France
- Reports of prolonged periods of fasting by Geyelin 1910-1920
- "Until the children can't stand it"
- Became popular in the USA (Michigan)

FASTING AS EPILEPSY CURE.

Osteopaths Hear That 22 Days on Water Usually End Fits.

LOS ANGELES, July 5.—Epilepsy may be cured by fasting, Dr. Hugh Conklin told the twenty-sixth annual convention of the American Osteopathic Association, now in session here. Epilepsy, according to Dr. Conklin, is caused by the improper functioning of certain glands in the bowels. By fasting for twenty-two days, taking only water, a cure may be effected, he said.

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July 27, 1921

- Anecdotal reports by Dr. Rawle Geyelin of benefits of fasting on seizure control 1910s
- Dr. Wilder at Mayo Clinic, Rochester, MN creates a high fat, low carbohydrate diet to mimic fasting state
- Highly popular in children and adults

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1990's – keto diet availability

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Charlie Foundation FOR KETOGENIC THERAPIES

THERAPIES LEARN AM I A CANDIDATE RECIPES STORE RESOURCES ABOUT

Photo of Charlie Abrams from Charlie Foundation website

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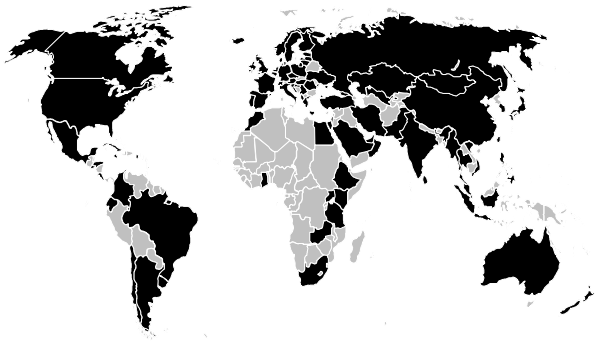
Countries where ketogenic diet is practiced



October 13, 2018

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Kossoff, et al. Epilepsia. 2005;46:280-9.; Kossoff, et al. Epilepsy Res. 2012;100:205-9.

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RESEARCH

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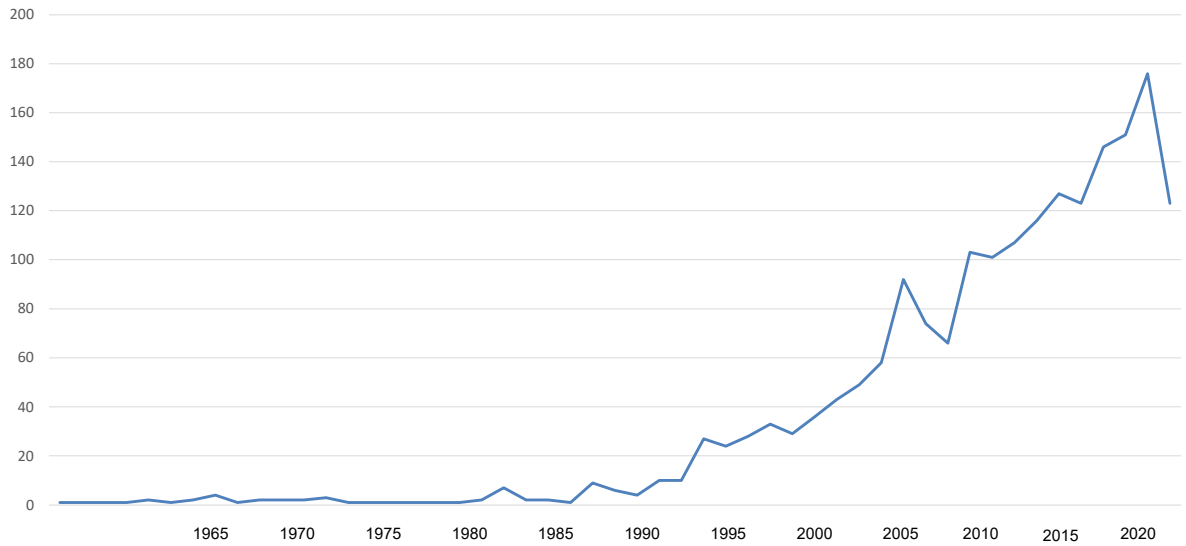
Ketogenic Diet Studies Published



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A blinded, crossover study of the efficacy of the ketogenic diet

Freeman JM, Vining EPG, Kossoff EH, et al. Epilepsia. 2009;50:322-5.

The ketogenic diet for the treatment of childhood epilepsy: a randomised controlled trial.

Neal EG, Chaffe H, Schwartz RH, et al. Lancet Neurology. 2008;7:500-6.

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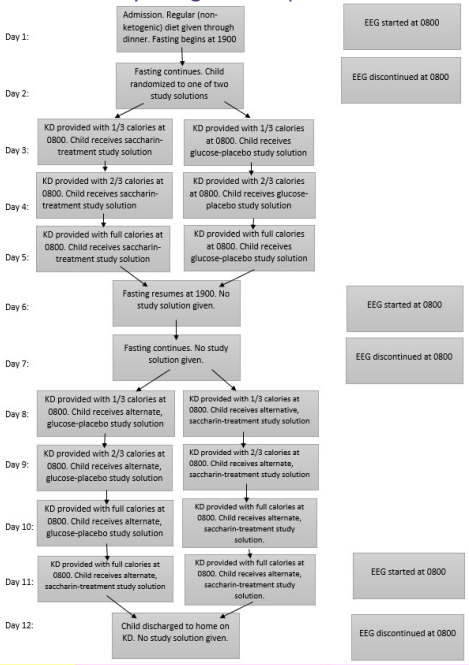
Hopkins Double-Blinded Study

- 12-day study period
  - Start of the diet
  - Children with Lennox-Gastaut Syndrome
- Trend towards saccharin superiority in clinical seizures (p=0.07)
  - Median -34 seizures/day over 12 days (p=0.003)
- Probably an inadequate placebo state due to fasting twice

Study Design and Implementation



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Flow chart adapted from Freeman JM, et al. *Epilepsia*. 2009;50:322-5.

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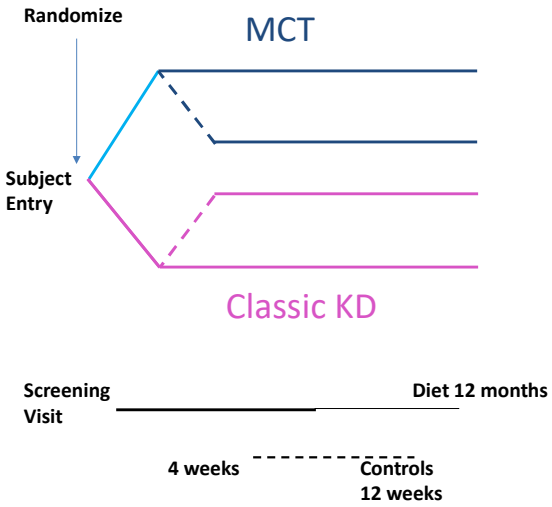
London Study



Slide courtesy of Dr. Helen Cross

Neal EG, et al. *Lancet Neurology.* 2008;7:500-6.

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International Guidelines established in 2009

Optimal clinical management of children receiving the ketogenic diet: Recommendations of the International Ketogenic Diet Study Group

Charlie FOUNDATION

Eric H. Kossoff, Beth A. Zupec-Kania, Per E. Amark, Karen R. Ballaban-Gil, A. G. Christina Bergqvist, Robyn Blackford, Jeffrey R. Buchhalter, Roberto H. Caraballo, J. Helen Cross, Maria G. Dahlin, Elizabeth J. Donner, Joerg Klepper, Rana S. Jehle, Heung Dong Kim, Y. M. Christiana Liu, Judy Nation, Douglas R. Nordli, Jr., Heidi H. Pfeifer, Jong M. Rho, Carl E. Stafstrom, Elizabeth A. Thiele, Zahava Turner, Elaine C. Wirrell, JamesW. Wheless, Pierangelo Veggiotti, Eileen P. G. Vining and The Charlie Foundation, and the Practice Committee of the Child Neurology Society

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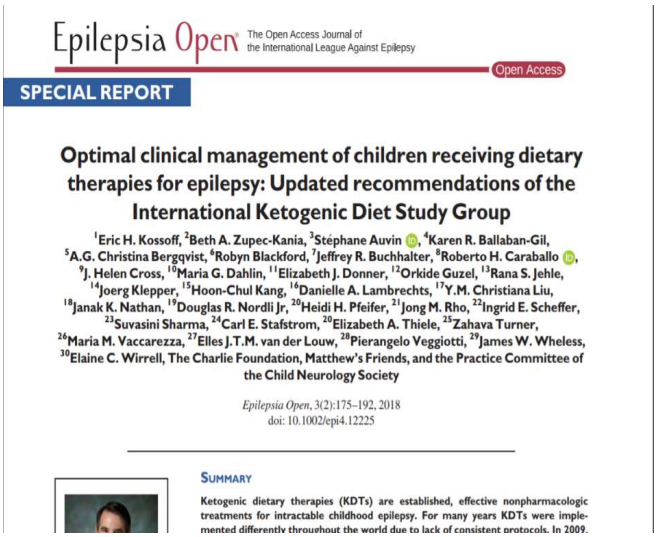
Clinical guidelines updated in 2018



Epilepsia Open The Open Access Journal of the International League Against Epilepsy

Open Access

SPECIAL REPORT

Optimal clinical management of children receiving dietary therapies for epilepsy: Updated recommendations of the International Ketogenic Diet Study Group

[1]Eric H. Kossoff, [2]Beth A. Zupec-Kania, [3]Stéphane Auvin, [4]Karen R. Ballaban-Gil, [5]A.G. Christina Bergqvist, [6]Robyn Blackford, [7]Jeffrey R. Buchhalter, [8]Roberto H. Caraballo, [9]J. Helen Cross, [10]Maria G. Dahlin, [11]Elizabeth J. Donner, [12]Orkide Guzel, [13]Rana S. Jehle, [14]Joerg Klepper, [15]Hoon-Chul Kang, [16]Danielle A. Lambrechts, [17]Y.M. Christiana Liu, [18]Janak K. Nathan, [19]Douglas R. Nordli Jr, [20]Heidi H. Pfeifer, [21]Jong M. Rho, [22]Ingrid E. Scheffer, [23]Suvasini Sharma, [24]Carl E. Stafstrom, [20]Elizabeth A. Thiele, [25]Zahava Turner, [26]Maria M. Vaccarezza, [27]Elles J.T.M. van der Louw, [28]Pierangelo Veggiotti, [29]James W. Wheless, [30]Elaine C. Wirrell, The Charlie Foundation, Matthew's Friends, and the Practice Committee of the Child Neurology Society

Epilepsia Open, 3(2):175–192, 2018
doi: 10.1002/epi4.12225

SUMMARY

Ketogenic dietary therapies (KDTs) are established, effective nonpharmacologic treatments for intractable childhood epilepsy. For many years KDTs were imple-
mented differently throughout the world due to lack of consistent protocols. In 2009.

Open access article

Kossoff, et al. Epilepsia Open. 2018;3:175-92.

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CKD basics

High fat diet
- 80-90% of total calories from fat

DRI protein needs

Low carbohydrate diet
- 2-5%

All foods weighed on a gram scale

Recipes prepared using computer program

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DRI = Dietary Reference Intake

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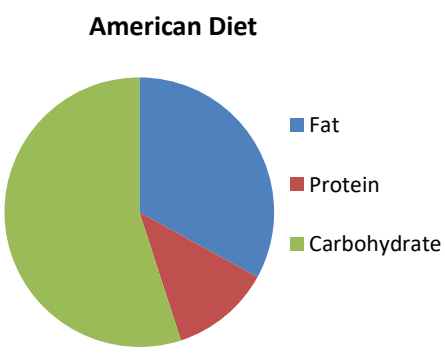
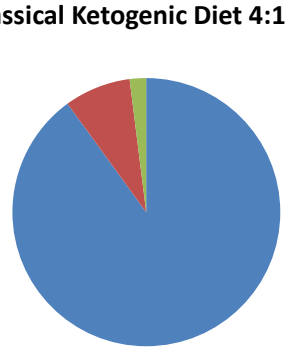
Comparison





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Who gets placed on the diet?

Table 1: Epilepsy Syndromes and conditions (listed alphabetically) for which the KD has been consistently reported as more beneficial (>70%) than the average 50% KD response (defined as >50% seizure reduction).
Angelman syndrome[56,57]
Complex 1 mitochondrial disorders[51,55]
Dravet syndrome[35,36]
Epilepsy with myoclonic–atonic seizures (Doose syndrome)[34,37,38]
Glucose transporter protein 1 (Glut-1) deficiency syndrome (Glut1DS)[27,29–32]
Febrile infection–related epilepsy syndrome (FIRES)[44–47]
Formula-fed (solely) children[48,49]
Infantile spasms[10,39,40]
Ohtahara syndrome[50–52]
Pyruvate dehydrogenase deficiency (PDHD)[28]
Super-refractory status epilepticus[44,46,53,54]
Tuberous sclerosis complex[41–43]
*full references available in article

Table 2: Several conditions (listed alphabetically) in which the KD has been reported moderately beneficial (not better than the average dietary response, or in limited single-center case reports)
Adenylosuccinate lyase deficiency[64]
CDKL5 encephalopathydisorders[67]
Childhood absence epilepsy[69]
Cortical malformation[73, 74]
Epilepsy of infancy with migrating focal seizures[68]
Epileptic encephalopathy with continuous spike-and-wave during sleep[70]
Glycogenosis type V[65]
Juvenile myoclonic epilepsy[66]
Lafora body disease[58]
Landau-Kleffner syndrome[61]
Lennox-Gastaut syndrome[26]
Phosphofructokinase deficiency[63]
Rett syndrome[59, 60]
Subacute sclerosing panencephalitis (SPSE)[62]
*full references available in article

- Patients who fail the traditional anti-convulsant therapy
- poor candidates for epilepsy surgery
- All ages
- Average time on diet 1-2 years

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Tables adapted from Kossoff, et al. Epilepsia Open. 2018;3:175-92.

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Table 3: Contraindications to the use of the KD
Absolute
Carnitine deficiency (primary)
Carnitine palmitoyl transferase (CPT) I or II deficiency
Carnitine translocase deficiency
β-oxidation defects
Medium-chain acyl dehydrogenase deficiency (MCAD)
Long-chain acyl dehydrogenase deficiency (LCAD)
Short-chain acyl dehydrogenase deficiency (SCAD)
Medium-chain 3-hydroxyacyl-CoA deficiency
Pyruvate carboxylase deficiency
Porphyria
Relative
Inability to maintain adequate nutrition
Surgical focus identified by neuroimaging and video-EEG monitoring
Parent or caregiver noncompliance
Propofol concurrent use (risk of propofol infusion syndrome may be higher)

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Table adapted from Kossoff, et al. Epilepsia Open. 2018;3:175-92.

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Meal Plan

Basic Structure	Typical menu
Heavy whipping cream	40g 36% heavy cream
Butter/mayonnaise/oil	21 g fat
Protein	24 g chicken breast
Fruit or vegetable	11 g broccoli
	12 g lettuce

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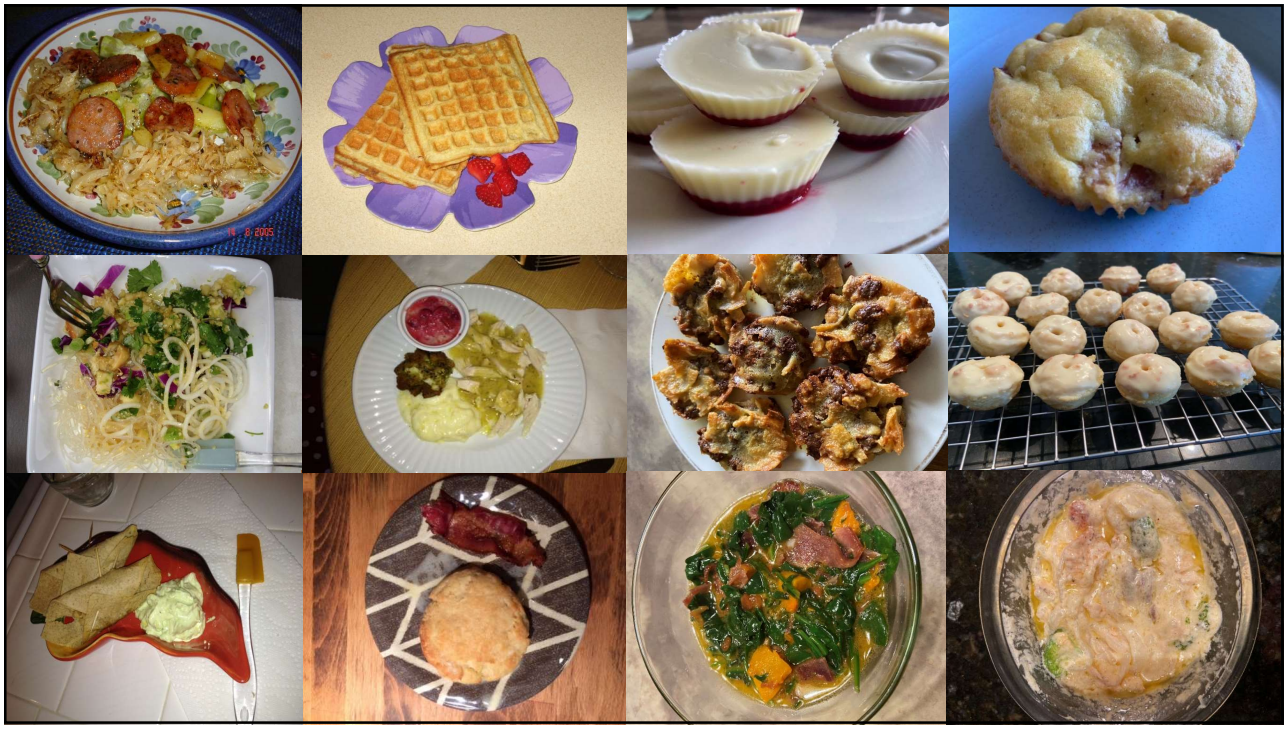

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Ketogenic formulas

KetoCal® (Nutricia North America)
- 2.5:1 LQ (Vanilla Flavored)
- 3:1 Powder (Unflavored)
- 4:1 Powder (Vanilla Flavored)
- 4:1 LQ (Flavored and Unflavored)

RCF® (Abbott) – Ross Carbohydrate Free Formula
- Soy formula

KetoVie® (Ajinomoto Cambrooke)
- 3:1 (Unflavored)
- 4:1 (Chocolate and vanilla flavors)
- 4:1 Peptide

Keto Peptide (Functional Formularies)
- 2.47:1 (Blended formula)

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Modular Products

Lipid
- Microlipid® (Nestlé) – safflower oil emulsion at 4.5 kcal/mL
- MCT Oil® (Nestlé) – fractionated coconut oil at 7.7 kcal/mL
- Liquigen® (Nutricia) – MCT emulsion at 4.5 kcal/mL
- Retail Oils (Olive oil, coconut oil) – variable caloric density

Carbohydrate
- Solcarb powder (Solace) – carbohydrate powder – maltodextrin - 3.75 kcal/g
- Polycal™ powder (Nutricia) – carbohydrate powder – maltodextrin – 3.84 kcal/g

Protein
- Beneprotein® (Nestlé) – whey protein powder – 6 gm protein in 7 gm powder
- Complete Amino Acid Mix (Nutricia) – 100% amino acid powder – 8.2 g protein in 10 g powder

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Supplementation

- Diet deficient in:
  - B Vitamins
  - Vitamin C
  - Calcium, zinc, phosphorous
  - Fiber
  - Trace minerals
  - Carnitine, selenium
- Supplement with carbohydrate free multivitamin and mineral supplement

Table 5: Supplementation recommended for children on the KD
Universal recommendations
Multivitamin with minerals (including trace minerals, especially selenium)
Calcium and vitamin D (meeting daily RDA requirements)
Optional extra supplementation
Vitamin D (above RDA)
Oral citrates (eg, CytraK or PolycitraK)
Laxatives (Miralax®, mineral oil, glycerin suppository)
Additional selenium, magnesium, zinc, phosphorus, iron, copper
Carnitine
MCT oil or coconut oil (source of MCT)
Salt (sodium to add to RCF formula if used for greater than age 1 year)
All supplements listed should be provided as carbohydrate-free preparations whenever possible.

Table adapted from Kossoff, et al. Epilepsia Open. 2018;3:175-92.

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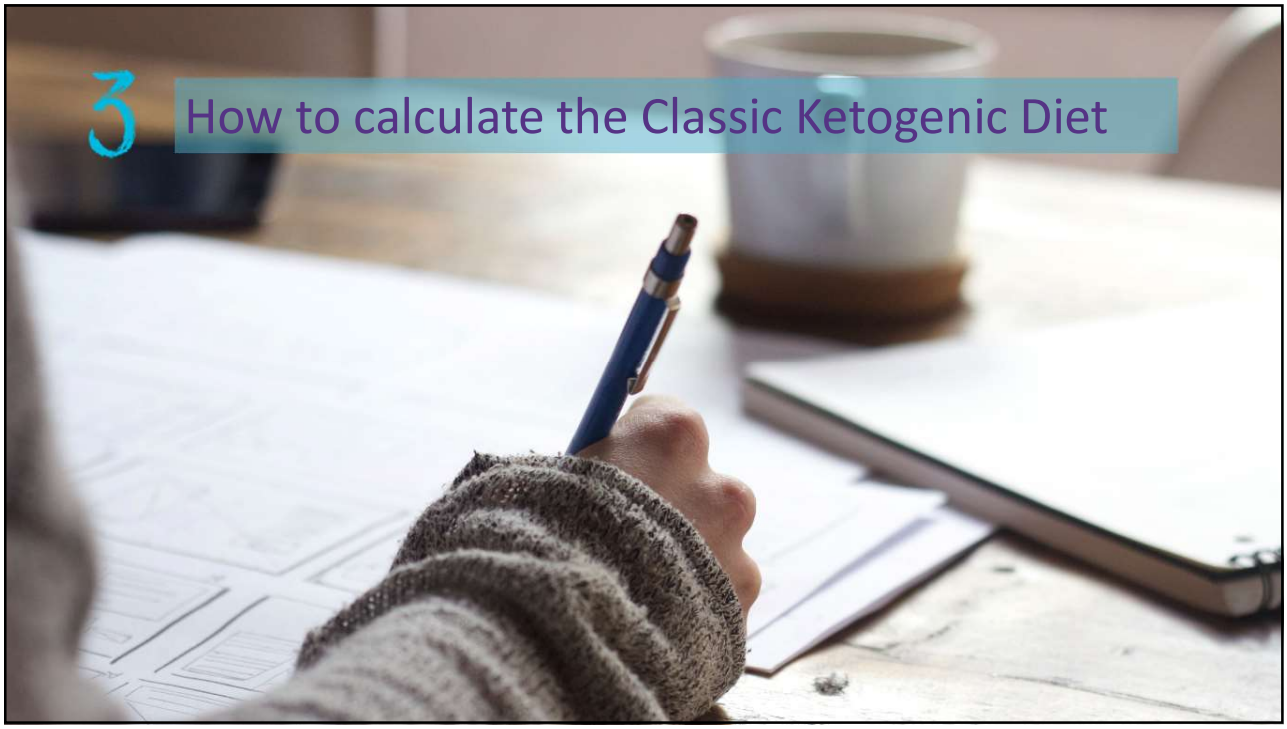

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Ratio

- Ratio: Grams of fat: protein and carbohydrate combined
  - Example: 4:1 ratio is 4 grams of fat to 1 gram of protein and carbohydrate combined
- Typical ratio and uses
  - 3:1 Children <2 years of age, teenagers & compromised patients
  - 4:1 > 2yo
- Higher the ratio the lower the amount of allowed protein and carbohydrates

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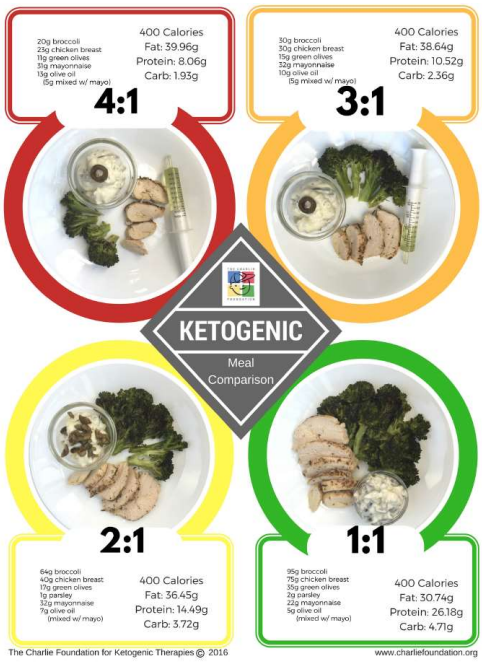

Handout from The Charlie Foundation

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Estimating Calories Protein & Fluid

Calories

- Dietary Reference Intake (DRI) + Activity Factor (AF)
  - Can use WHO, Scofield…
- 3-day food record
  - Important to compare estimated needs with food record and growth history
- No calorie restriction
- Use clinical judgment regarding patients with obesity and failure to thrive

Protein

- DRI

Fluid

- Maintenance fluid calculation
- No fluid restrictions

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Calculating Dietary Units

Ratio	Calories per Dietary Unit	Example
2:1	22	**(2X9) + (1X4) =22**
3:1	31	**(3X9)+ (1X4) =31**
4:1	40	**(4X9)+ (1X4) =40**
5:1	49	**(5X9) +(1X4)=49**

By dividing the dietary units of a given ratio into the determined total calories (age x calories per kg) the total grams of protein, carbohydrate, and fat in a given ketogenic diet can be determined.

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Keto Admission

JHH Admission Protocol

- 4 families at a time
- Admission 3 days (Monday-Wednesday)
- Education Daily
- Blood Glucose levels monitored
- Ketone levels

Typical process

- **Initiate KD slowly**:
  - 24 hour fast (optional, but usually done in >2 years old)
- **Goal ratio at 1/2 calorie strength for 24 hours**
  - Eggnog or ketogenic formula until full strength
- **Advance to Full Strength**
  - With actual food

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Daily Education

Day	Topics Covered
Monday	• **MD review** • **Diet basics** • **Side Effects** • **Diet initiation schedule** • **Meet with floor team/nurses**
Tuesday	• RD: The basics of the ketogenic diet • Meal Plan Guidelines • Social worker meeting
Wednesday	• **Ketogenic Computer program** • **What to do when your child gets sick** • **Parent lecture** • **Weighing and measuring foods** • **Learning how to read recipes**

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Side Effects

- Constipation
- Poor growth
- Osteopenia/ osteoporosis
- Kidney stones
- Hyperlipidemia
- Vitamin and mineral deficiency

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Follow-up

Generally every 3 months for the initial year
- Children less than 2 years seen in 1 month
- Labs at each visit
  - CMP, Fasting lipid panel, urinalysis, Vit D, selenium

Medications usually not changed the first month

Frequent phone and email contact in between clinic visits

At our center, all management through the keto team from now on

Table adapted from Kossoff, et al. Epilepsia Open. 2018;3:175-92.

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Table 6: Recommendations for aspects of a follow-up KD clinic visit

Nutritional assessment (registered dietitian)	
Height, weight, ideal weight for stature, growth velocity, BMI when appropriate	
Head circumference (when appropriate)	
Review appropriateness of KD prescription (calories, protein, and fluid)	
Review vitamin and mineral supplementation	Assess compliance to KD
Adjust KD, if necessary, to improve compliance and seizure control	
Medical evaluation (neurologist)	
Efficacy of the diet (is the KD meeting parental expectations?)	
Side effects of the KD	Antiseizure drug reduction (if applicable)
Should KD be continued?	
Laboratory assessment	
Complete blood count with platelets	
Electrolytes to include serum bicarbonate, total protein, calcium	
Serum liver and kidney profile (including albumin, blood urea nitrogen, creatinine)	
Vitamin D level	Fasting lipid profile
Free and total carnitine	Selenium level
Urinalysis consideration)	EEG (at KD discontinuation
Anticonvulsant drug levels (if applicable)	
Optional	
Serum beta-hydroxybutyrate (BOH) level	Urine calcium and creatinine
Zinc, copper levels	Renal ultrasound
ECG (Electrocardiogram) Bone mineral density (DEXA scan) after 2 years on the KD	

**Visits should be at least every 3 months for the first year of the KD, with a visit 1 month after starting the KD also advised

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Other Diet Variants for Epilepsy

- Modified Atkins Diet
- Low Glycemic Index Diet
- MCT oil Diet
- Modified Ketogenic Diet

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Comparison

Modified Atkins Diet

- No calorie or protein restriction
- No weighing on gram scale
- Stress the importance of fat in the diet

Low Glycemic Index Diet

- Focus on low glycemic index carbohydrates <50
- Allowed a lot more carbohydrates

MCT Oil Diet

- Uses medium chain triglycerides (MCT oil) in place of the large amounts of cream & butter to allow more room for carbs and protein
- Based on percentages of calories vs. ratio's (ex. 30-60% MCT oil, 10% carb, 12% protein or 2 x RDA, 18-48% fat). Total fat=70-80%*
- Calories **not** restricted, based on RDA's or individual needs

Modified Ketogenic Diet

- Low and slow
- Start off at a low ratio and slowly increase as needed

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Johns Hopkins Adult Epilepsy Diet Center: Modified Atkins Diet Protocol

Pre-Diet

- Nutrition evaluation – 3-day food record, anthropometrics
- Laboratory values – CMP, CBC, fasting lipids
- Medications levels
- Diagnostic studies: EEG, MRI..
- Screening for cardio and cerebrovascular risk factors, history of kidney stones

Initiation

- 20 g of carbohydrates
- No calorie restriction
- MVI, Calcium and Vitamin D
- Seizure calendar
- Urine ketones
- Weight
- Start and end of menses

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Summary

- Ketogenic diet involves time and dedication on the dietitian's part
  - – not difficult but time consuming
- Requires a team
  - – Physician, RN, Pharmacy support…

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References

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Q & A

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